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APPLICATION NO.	FILING DATE	FIRST NAMED INVENTOR	ATTORNEY DOCKET NO.	CONFIRMATION NO.
09/378,577	08/20/1999	WENYUAN SHI	60307-5001	9309

7590 07/25/2002

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EXAMINER	
ZEMAN, ROBERT A	
ART UNIT	PAPER NUMBER
1645	16

DATE MAILED: 07/25/2002

Please find below and/or attached an Office communication concerning this application or proceeding.

Office Action Summary	Application No. 09/378,577	Applicant(s) SHI ET AL.	
	Examiner Robert A Zeman	Art Unit 1645	

-- The MAILING DATE of this communicati n appears on the cover sheet with the correspondence address --

Period for Reply

A SHORTENED STATUTORY PERIOD FOR REPLY IS SET TO EXPIRE 3 MONTH(S) FROM THE MAILING DATE OF THIS COMMUNICATION.

- Extensions of time may be available under the provisions of 37 CFR 1.136(a). In no event, however, may a reply be timely filed after SIX (6) MONTHS from the mailing date of this communication.
- If the period for reply specified above is less than thirty (30) days, a reply within the statutory minimum of thirty (30) days will be considered timely.
- If NO period for reply is specified above, the maximum statutory period will apply and will expire SIX (6) MONTHS from the mailing date of this communication.
- Failure to reply within the set or extended period for reply will, by statute, cause the application to become ABANDONED (35 U.S.C. § 133).
- Any reply received by the Office later than three months after the mailing date of this communication, even if timely filed, may reduce any earned patent term adjustment. See 37 CFR 1.704(b).

Status

1)☒ Responsive to communication(s) filed on *20 May 2002* .

2a)☒ This action is **FINAL**. 2b)☐ This action is non-final.

3)☐ Since this application is in condition for allowance except for formal matters, prosecution as to the merits is closed in accordance with the practice under *Ex parte Quayle*, 1935 C.D. 11, 453 O.G. 213.

Disposition of Claims

4)☒ Claim(s) *1-4,6-10,12 and 17* is/are pending in the application.

4a) Of the above claim(s) _____ is/are withdrawn from consideration.

5)☐ Claim(s) _____ is/are allowed.

6)☒ Claim(s) *1-4,6-10,12 and 17* is/are rejected.

7)☐ Claim(s) _____ is/are objected to.

8)☐ Claim(s) _____ are subject to restriction and/or election requirement.

Application Papers

9)☐ The specification is objected to by the Examiner.

10)☐ The drawing(s) filed on _____ is/are: a)☐ accepted or b)☐ objected to by the Examiner.

Applicant may not request that any objection to the drawing(s) be held in abeyance. See 37 CFR 1.85(a).

11)☐ The proposed drawing correction filed on _____ is: a)☐ approved b)☐ disapproved by the Examiner.

If approved, corrected drawings are required in reply to this Office action.

12)☐ The oath or declaration is objected to by the Examiner.

Priority under 35 U.S.C. §§ 119 and 120

13)☐ Acknowledgment is made of a claim for foreign priority under 35 U.S.C. § 119(a)-(d) or (f).

a)☐ All b)☐ Some * c)☐ None of:

1.☐ Certified copies of the priority documents have been received.

2.☐ Certified copies of the priority documents have been received in Application No. _____ .

3.☐ Copies of the certified copies of the priority documents have been received in this National Stage application from the International Bureau (PCT Rule 17.2(a)).

* See the attached detailed Office action for a list of the certified copies not received.

14)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. § 119(e) (to a provisional application).

a) ☐ The translation of the foreign language provisional application has been received.

15)☐ Acknowledgment is made of a claim for domestic priority under 35 U.S.C. §§ 120 and/or 121.

Attachment(s)

1) ☐ Notice of References Cited (PTO-892)
2) ☐ Notice of Draftsperson's Patent Drawing Review (PTO-948)
3) ☐ Information Disclosure Statement(s) (PTO-1449) Paper No(s) _____ .
4) ☐ Interview Summary (PTO-413) Paper No(s). _____ .
5) ☐ Notice of Informal Patent Application (PTO-152)
6) ☐ Other: .

DETAILED ACTION

The amendment and response filed on 5-20-2002 is acknowledged. Claims 1-3, 6-9 and 12 have been amended. Claims 5, 11 and 13-16 have been canceled. Claims 1-4, 6-10, 12 and 17 are pending and currently under examination.

Claim Rejections Withdrawn

The rejection of claims 5, 11 and 13-16 under 35 U.S.C. 112, first paragraph, because the specification, while being enabling for the topical treatment using chimeric monoclonal antibodies, does not reasonably provide enablement for the treatment for the oral ingestion of tissue from transformed host is withdrawn. Cancellation of said claims has the rejection moot.

The rejection of claims 3 and 9 under 35 U.S.C. 112, second paragraph, as being vague and indefinite through the use of the phrase "step of preparing" is withdrawn in light of the amendment thereto.

The rejection of claims 1, 6 and 7 under 35 U.S.C. 102(b) as being anticipated by Lehner (U.S. Patent 5,352,446) is withdrawn in light of the amendment thereto.

Claim Rejections Maintained

35 USC § 103

The following is a quotation of 35 U.S.C. 103(a) which forms the basis for all obviousness rejections set forth in this Office action:

> (a) A patent may not be obtained though the invention is not identically disclosed or described as set forth in section 102 of this title, if the differences between the subject matter sought to be patented and the prior art are such that the subject matter as a whole would have been obvious at the time the invention was made to a person having ordinary skill in the art to which said subject matter pertains. Patentability shall not be negatived by the manner in which the invention was made.

This application currently names joint inventors. In considering patentability of the claims under 35 U.S.C. 103(a), the examiner presumes that the subject matter of the various claims was commonly owned at the time any inventions covered therein were made absent any evidence to the contrary. Applicant is advised of the obligation under 37 CFR 1.56 to point out the inventor and invention dates of each claim that was not commonly owned at the time a later invention was made in order for the examiner to consider the applicability of 35 U.S.C. 103(c) and potential 35 U.S.C. 102(e), (f) or (g) prior art under 35 U.S.C. 103(a).

The rejection of claims 1-4, 6-10, 12 and 17 under 35 U.S.C. 103(a) as being unpatentable over Ma et al. (European Journal of Immunology 1994 Vol. 24 (1) pages 131-138) in view of Adair et al (U.S. Patent 5,877,293) is maintained for reasons of record.

Applicant argues:

1. Ma et al. teach away from the claimed instant invention since Ma et al. uses a different approach than that used by present invention.

2. Ma et al. antibodies prevent dental caries by causing bacterial aggregation as opposed to inducing a humoral immune response.

3. The modification disclosed by Ma et al. is directed to replcacing the Fc portion of the IgG with the Fc portion of the IgA since IgA is considered to be more effective than IgG in preventing bacterial colonization.

4. Ma et al. disclose that Fc-mediated humoral response is not essential in preventing bacterial colonization.

5. In light of the disclosure of Ma et al. it would not be obvious to one skilled in the art that he could treat or prevent dental caries by using the methodology of the instant invention.

6. Even if one of skill in the art decided to experiment with humoral responses in treating or preventing dental caries, he would have no expectation of success since it is well known that mucosal surfaces lack IgG and IgM antibodies that are required to activate antibody-dependent cell-mediated cytotoxicity or complement-dependent cytolysis.

7. The disclosure of Adiar et al. does not cure the deficiencies of Ma et al. since it fails to teach the use of chimeric antibodies to treat dental caries by eliciting a humoral immune response.

Applicant's arguments have been fully considered and deemed non-persuasive.

Contrary to Applicant's assertion that Ma et al. merely discloses the use of IgA based antibodies to treat dental caries, Ma et al also disclose IgG based antibodies. For example, in the Abstract Ma et al. clearly state "the results demonstrate that IgA **as well as IgG class antibodies assembled** correctly..." and in the Introduction Ma et al. state that Guy's 13 is a murine **IgG1** class of antibody that recognizes the 185 kDa cell-surface protein of *Streptococcus mutans.* Additionally, Ma et al. disclose that three different forms of Guy's 13 antibody was expressed in plants including Guys's 13 **IgG1** with the original gamma heavy chain (see page 132). Said antibodies would, by their very nature stimulate a humoral immune response regardless of the motivation behind its application. Therefore, as previously stated in the previous office action, Ma et al. disclose methods for the production of chimeric monoclonal antibodies against *Staphylococcus mutans* in transgenic tobacco plants to be used in the treatment of dental caries in humans and other mammals (see page 131, second paragraph). The disclosed methods include:

the cloning of heavy and light chain genes (see page 132); plant transformation and regeneration (see page 132); antibody chain detection (see pages 132-133); and measurement of chimeric antibodies and their binding capacities (see pages 133-134). Ma et al. differs from the claimed inventions in that both the heavy and light chains of the chimeric monoclonal antibodies are derived from murine antibodies. However, Adair et al. disclose methods for the production of chimeric antibodies where the light chains are derived from murine antibodies and the heavy chains are derived from human antibodies. Consequently, it would have been obvious to one of skill in the art at the time the invention was made to use the methods of Adair et al. to "humanize" the chimeric antibodies disclosed in the methods of Ma et al. in order to take advantage of the reduced antigenicity and the increased therapeutic effectiveness of "humanized" (chimeric) antibodies. This "humanizing" consists of replacing the murine heavy chain sequences of Ma et al. with the human heavy chain sequences of Adair et al. in the expression vectors of Ma et al. It should be noted that humanizing antibodies is a standard procedure used in most immunology laboratories. That, and coupled with the fact that Ma et al. suggests "incorporating other regions such as the complement binding region of human IgG" (see page 137, second paragraph) and Adair et al. state that chimeric monoclonal antibodies are less antigenic to humans and hence more effective therapeutically (see column 1 lines 52-65), one would have a high expectation of success in making the required antibodies and using them to treat or prevent dental caries.

Applicant is reminded that the aforementioned rejection is based on the combination of the cited references (see above) and not independently. Said combination clearly encompasses all the

limitations of the claimed invention. Additionally, as previously pointed out by Applicant, the construction of chimeric and humanized antibodies and the tailoring of the constant regions (i.e. selection of isotypes specific for cell mediated cytotoxicity) are well known in the art (see Kipriyanov et al., Molecular Biology, Vol. 12, pages 173-201).

New Claim Objections

Claims 3 and 9 are objected to because of the following informalities: Applicant has amended said claims to recite "step c" of an antecedent claims. Said claims recite "step c)" not "step c". Appropriate correction is required.

Conclusion

No claim is allowed.

Applicant's amendment necessitated the new ground(s) of objection presented in this Office action. Accordingly, **THIS ACTION IS MADE FINAL**. See MPEP § 706.07(a). Applicant is reminded of the extension of time policy as set forth in 37 CFR 1.136(a).

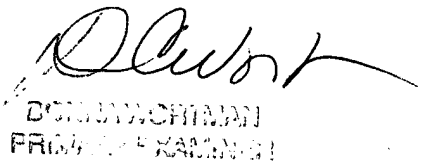
A shortened statutory period for reply to this final action is set to expire THREE MONTHS from the mailing date of this action. In the event a first reply is filed within TWO MONTHS of the mailing date of this final action and the advisory action is not mailed until after the end of the THREE-MONTH shortened statutory period, then the shortened statutory period will expire on the date the advisory action is mailed, and any extension fee pursuant to 37 CFR 1.136(a) will be calculated from the mailing date of the advisory action. In no event,

however, will the statutory period for reply expire later than SIX MONTHS from the date of this final action.

Any inquiry concerning this communication or earlier communications from the examiner should be directed to Robert A Zeman whose telephone number is (703) 308-7991. The examiner can normally be reached on M-Th 7:30 am - 5:00 pm and Alternate Fridays.

If attempts to reach the examiner by telephone are unsuccessful, Donna Wortman, Primary Examiner, can be reached on (703) 308-1032. The fax phone numbers for the organization where this application or proceeding is assigned are (703) 308-4242 for regular communications and (703) 308-4242 for After Final communications.

Any inquiry of a general nature or relating to the status of this application or proceeding should be directed to the receptionist whose telephone number is (703) 308-0196.



Robert A. Zeman
July 24, 2002